

# **The Use of Organic Germanium in Chronic Epstein-Barr Virus Syndrome (CEBVS): An Example of Interferon Modulation of Herpes Reactivation**

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The organogermanium compound bis carboxyethyl germanium sesquioxide, or Ge-132, has been found to provide relief for many patients from the often debilitating symptoms of the Chronic Epstein-Barr Virus Syndrome (CEBVS), an affliction that may be affecting millions of Americans. CEBVS is also referred to as Chronic Fatigue Syndrome by many physicians, including the Center for Disease Control (CDC), because fatigue is the main symptom and Epstein Barr Virus has not yet been established as the sole etiological agent.

Initial reports on the clinical success of organic germanium in patients with CEBVS were presented by Jeffrey Anderson, M.D., at the Orthomolecular Medical Society meetings in February 1987.<sup>1</sup> 500 mg/day sublingually in divided doses provided relief from fatigue and depression and the amelioration of other chronic symptoms.

He later found that response to Ge-132 varied. Nearly half of the patients derived little relief from their chronic fatigue and malaise, even when the daily dose was increased to up to one gram. Nevertheless, half of his patients were responding favourably, although the amount of Ge-132 required to initiate or maintain distinct improvement also varied. Some patients needed to take 1000 mg before they felt a distinct improvement. He found that at least 20% of those CEBV patients who tried Ge-132 continued to show dramatic improvement.

Dr. Arnold Horowitz, a psychotherapist from Beverly Hills was stricken with CEBVS, and disabled for a year and a half. Responding dramatically to Ge-132, he now introduces it to his patients suffering from fatigue, malaise and depression.

Ron Greenberg, M.D., has found in his Vancouver practice that among patients

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with clinical and laboratory evidence of CEBVS, about 25% show "substantive clinical improvement" with 300 mg Ge-132/day. George Maslen M.D., of New York started including Ge-132 in his nutritional immune support program for CEBVS patients several months ago. He also noticed that patient response to Ge-132 was favourable but variable. He found that 150-300 mg/day of Ge-132 provided significant relief from CEBVS symptoms in the majority of his patients. Some start to respond at higher dosages and occasionally a patient may require one gram/day to obtain marked relief. He finds 1/5 are non-responders who do not seem to derive any benefit from Ge-132.

Dr. Anderson thinks Ge-132 works synergistically with other immune stimulant nutrients. He works with a full complement of nutritional supplements, and finds that almost all of his patients seem to improve on a CoQ<sub>10</sub> (Coenzyme Q<sub>10</sub>), DMG (N,N'dime-thylglycine), Ge-132 combination. In a few individual cases patients who formerly needed high doses of Ge-132 in order to feel improvements were able to get the same effect at a much lower dose when CoQ<sub>10</sub> and DMG were added.

The severity of symptoms varies considerably in patients with CEBVS, some people are minimally affected, while others are incapacitated by fatigue, depression and continual flu-like symptoms. The CDC considers CEBVS or "Chronic Fatigue Syndrome" to be related to some combination of viruses of the herpes family, which includes: Herpes Simplex 1 and 2 which cause oral and genital lesions; Cytomegalovirus which can transactivate HIV and may contribute to the clinical manifestations of AIDS; Varicella Zoster which causes chicken pox and shingles; Epstein-Barr Virus which causes infectious mononucleosis; and Human B-Lymphotropic Virus, which was

only recently discovered in 1986. Apparently it is not uncommon for patients with Chronic Fatigue Syndrome to have elevated antibodies titers to several herpes viruses.<sup>2 3</sup>

Most North Americans are infected by EBV, making it one of the most widespread infectious agents known. Antibodies are usually produced during childhood exposures without clinical symptoms. Infection in the 2nd or 3rd decades often lead to bouts with infectious mononucleosis. Regardless, the virus persists in a latent or dormant carrier state, establishing a complex lifelong relationship with the host. In an immune-compromised individual EBV can become reactivated if the host-virus balance is perturbed.<sup>4</sup>

Predictably, reactivation of herpes is a common occurrence in cancer patients and transplant patients in whom non-specific cellular immunity is deficient. The onset of CEBVS is frequently associated with periods of physical or emotional stress, as are episodes of increased symptomatology.

Immune depression resulting from overactive suppressor cells could account for subtle changes in responsiveness that precede herpes virus reactivation.

Clinical Herpes virus reactivation and dissemination can also be correlated with the extent of depressed cellular or humoral immunity to the specific virus. This has been shown with Varicella Zoster virus reactivation in groups of immuno suppressed patients.<sup>5</sup> The lower the specific immunity the more readily the virus is reactivated.

Herpes viruses seem to be particularly sensitive to interferons *in vitro* and *in vivo*. The cessation of the dissemination of zoster virus to distant sites has correlated directly with the appearance of interferon in vesicle fluid.<sup>6</sup> Thus endogenous interferon appears to promptly halt the spreading virus.

There may be a deficit in the interferon response mechanism in many types of immuno suppressed patients, including those with CEBVS.

Exogenous interferon has been effective in suppressing reactivation of latent herpes viruses in several clinical trials.<sup>7</sup> In controlled studies human leukocyte interferon was found to block Herpes Zoster reactivation in cancer patients and Cytomegalovirus reactivation in renal and bone

marrow transplant recipients. Clinical trials with interferon in CEBVS patients have not been carried out.

Organic germanium may repress CEBVS because of its ability to stimulate endogenous interferon.

Ge-132 has many remarkable biological properties. The best studied effects have been on the mammalian immune system on which it has a number of augmenting effects, at least some of which are a consequence of host production of interferon. In all animals tested, including humans, there is a dose dependent increase in serum levels of gamma interferon in response to Ge-132.<sup>8 9 10</sup>

Gamma interferon is primarily a lympho-kine and modulates immunological activity by increasing the availability of Natural Killer cells and activating macrophages, the prime cellular immunological weapons against viral and other infections as well as malignant cells.

It is certainly possible that other lympho-kines are involved in Ge-132's immuno-modulating activity but there is little doubt about gamma interferon.

The immunomodulating activity of G-IFN and Ge-132 are identical, including the specific types or subsets of T-cells activated or inhibited, and the time course of INF stimulation by Ge-132 correlates with the expected immunomodulation activity.

In Japan Ge-132 is used clinically for a number of viral diseases including AIDS. It has been used to control latent Herpes Zoster reactivation, so it is not surprising that Ge-132 is effective in latent EBV infection. It is not known if the variable response of CEBVS patients to Ge-132 can be correlated with any of the variables of the disease syndrome such as duration or severity. Differences in the degree of infection or in immunological parameters of the virus-host balance could account for differences in response. Also, those less responsive to Ge-132 may be producing lesser amounts of interferon or other lymphokines. More research will be needed in order to determine the optimal use of Ge-132 in CEBVS. Considering the sound scientific basis for its action, the reported clinical success and its lack of toxicity, a person with CEBVS would be well advised to give Ge-132 a rigorous trial for at least two months.

Ge-132 would also be an important addition

to any nutritional regime in support of the immune system.

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